Selenium-Containing Heterocycles From Isoselenocyanates: Synthesis of 1,3-Selenazolidine and Perhydro-1,3-selenazine Derivatives

Sommen, Geoffroy L ; Linden, Anthony ; Heimgartner, Heinz

Abstract: Treatment of -halo alkylamines 9 and 10 with aryl and alkyl isoselenocyanates 6a–g in the presence of triethylamine in dichloromethane gave the corresponding 1,3-selenazolidines 11a–g and perhydro-1,3-selenazines 12a–g, respectively, in good to excellent yields. Chemical and spectroscopic evidence for the structures of all new compounds are presented, and in selected examples the molecular structures have been established by X-ray crystallography. The analogous reactions with isothiocyanates have been used for the preparation of 1,3-thiazolidines and perhydro-1,3-thiazines.

DOI: https://doi.org/10.1002/ejoc.200500090

Selenium-Containing Heterocycles From Isoselenocyanates: Synthesis of 1,3-Selenazolidine and Perhydro-1,3-selenazine Derivatives

Geoffroy L. Sommen,[a,b] Anthony Linden,[a] and Heinz Heimgartner*[a]

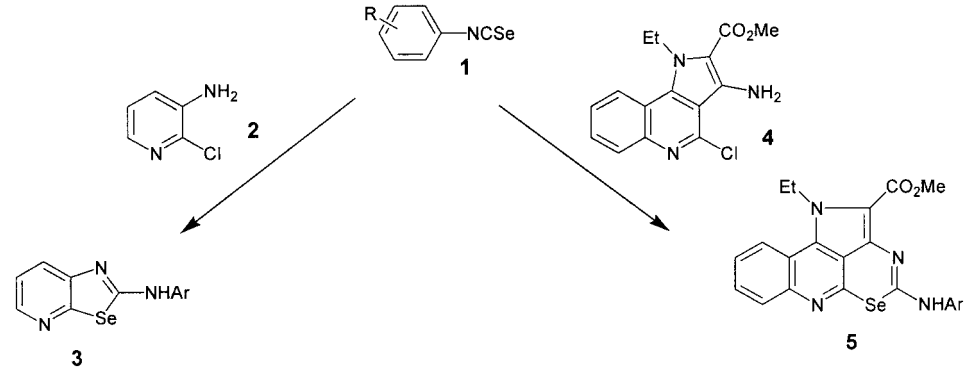
Keywords: Cyclizations / Isoselenocyanates / Selenium heterocycles / Sulfur heterocycles / X-ray crystallography

Treatment of ω-halo alkylamines **9** and **10** with aryl and alkyl isoselenocyanates **6a–g** in the presence of triethylamine in dichloromethane gave the corresponding 1,3-selenazolidines **11a–g** and perhydro-1,3-selenazines **12a–g**, respectively, in good to excellent yields. Chemical and spectroscopic evidence for the structures of all new compounds are presented, and in selected examples the molecular structures have been established by X-ray crystallography. The analogous reactions with isothiocyanates have been used for the preparation of 1,3-thiazolidines and perhydro-1,3-thiazines.

Introduction

The chemistry of organoselenium compounds has attracted much attention, not only because of strong interest in these compounds as synthetic tools[1–8] but also as a result of their unique biological[9,10] and medicinal activities.[11–19] Hatfield[20] demonstrated the wide importance of organoselenium compounds in human health, especially in cancer chemoprevention,[21] in food,[22–24] and in plants.[25,26] Although syntheses of thiazines[27] and oxazines[28,29] are well known, those of the corresponding selenazines have been limited, owing to difficulties in the preparation of the selenium-containing starting materials. Like many other syntheses of selenium-containing heterocycles, they involve the use of toxic selenium reagents, which are often difficult to handle. Isoselenocyanates[30–32] are very useful starting materials in heterocyclic chemistry[33] because they are easy to prepare[34] and can be stored.

Selenazines have attracted much attention not only in medicinal fields (antibacterial effects against *Escherichia coli* and *Staphylococcus aureus*,[35] inhibitory effect on the proliferation of human HT-1080 fibrosarcoma cells,[36] protein kinase inhibition,[37] and as antitumor agents[38]), but also as dyes.[39,40] Nevertheless, the preparation of this ring system is not well described in the literature, and only recently have some reports and reviews on the synthesis and applications of selenazines been published.[39,40] Similarly, selenazoles have attracted attention in the chemistry of dyestuffs,[41,42] as well as in medicine (antiinfective,[36] antiviral,[43] and antitumor agents[44]).



Scheme 1.

To the best of our knowledge, only a few papers describe the preparation of nonfused selenazoles from an isoselenocyanate[45–48] and, surprisingly, only one selenazole derivative prepared from a primary amine has been described.[49]

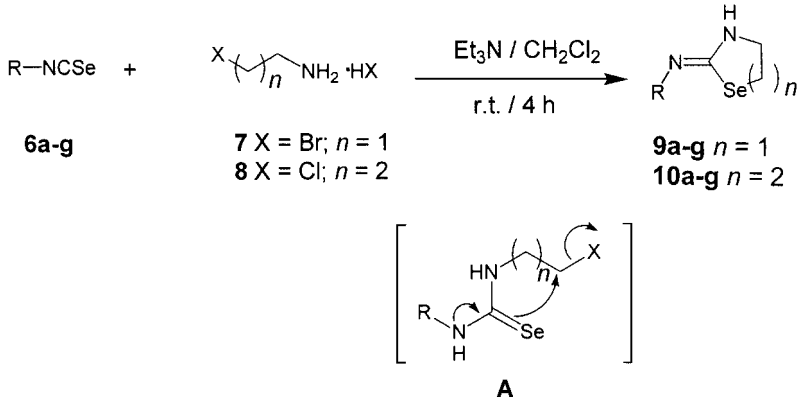
[a] Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, 8057 Zürich, Switzerland
Fax: +41-44-635-6836
E-mail: heimgart@oci.unizh.ch
[b] Postdoctoral stay at the University of Zürich, Winterthurerstrasse 190, 8057 Zürich, Switzerland

We have recently shown that aryl isoselenocyanates **1** are convenient precursors for the introduction of selenium into five- and six-membered selenaheterocycles of types **3**[50] and **5**,[51] respectively (Scheme 1). The aromatic starting materials **2** and **4** for these reactions each bore a primary amino group and a halogen atom. The formation of *1H*-1,3,6-triazaaceanthrylene derivatives **5** occurred on heating of **1** and **4** in boiling pyridine without any additional reagents. Similarly, 2-arylamino selenazolo[5,4-*b*]pyridines **3** were prepared from **1** and **2** in propan-2-ol at reflux. In the latter case, however, the product was obtained as the hydrochloride, which was very stable and gave the free amine derivative only with difficulty.

As a continuation of our studies in isoselenocyanate chemistry[50–57] we investigated the synthesis of five- and six-membered Se/N-heterocycles: 1,3-selenazoles and 1,3-selenazines. In this paper we report on reactions of aryl and alkyl isoselenocyanates **1** with the ω-halogeno alkylamines **9** and **10**.

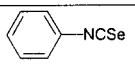
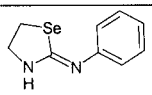
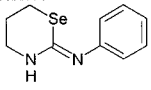
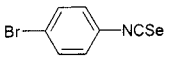
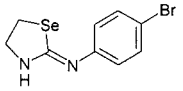
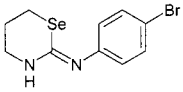
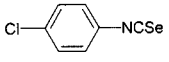
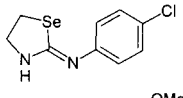
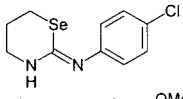
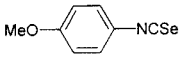
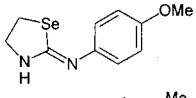
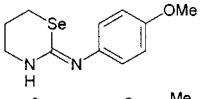
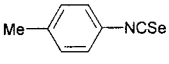
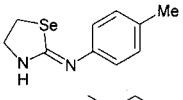
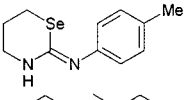
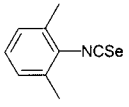
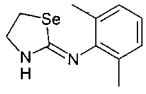
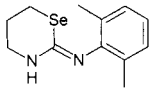
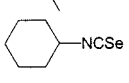
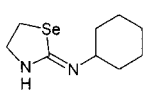
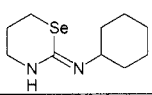
Results and Discussion

The halogenoamine (HX salt, one equiv.) was added to a stirred solution of the appropriate freshly prepared isoselenocyanate **6** in dry dichloromethane, followed by two equiv. of triethylamine. The isoselenocyanates **6** used were easily prepared from the corresponding *N*-arylformamides by treatment with phosgene and elemental selenium, by the procedure published by Barton et al.[34a] Stirring of the solution of **6** and **7** or **8** at room temperature for 4 h (except for cyclohexyl isoselenocyanate: 12 h) resulted in the formation of the selenium-containing heterocycles **9** and **10**, respectively, isolated in 39–96% yields (Scheme 2, Table 1).



Scheme 2.

Table 1. Preparation of 1,3-selenazolidines **9** and 1,3-selenazines **10** from isoselenocyanates **6**.

Entry	6	9	Yield (%)	10	Yield (%)
a			65		88
b			96		94
c			85		79
d			65		92
e			71		87
f			39		88
g			39		92

As shown in Table 1, the yields of the six-membered heterocycles **10** were, in general, higher than those of the corresponding five-membered heterocycles. Quite large differences were observed between **9f** and **10f** and between **9g** and **10g**, the two cases in which the steric hindrance between the residue at the imine N-atom and the heterocycle is the greatest.

We propose the following reaction mechanism for the formation of **9** and **10**: addition of the primary amino group to **6** produces a selenourea derivative **A**, which undergoes a cyclization step to give the heterocyclic product. In this one-pot, multi-step procedure, the cascade needs two equivalents of base. Triethylamine was chosen for its softness and for the ease of its elimination by washing the reaction mixture with water.

The structures of the selenazolidin-2-imines **9** were assigned on the basis of their spectroscopic data and elemental analyses. The crystal structures of **9a** and **9d** were also established by X-ray crystallography (Figure 1 and Figure 2). The products are 1,3-selenazolidines, each with an exocyclic C,N double bond.

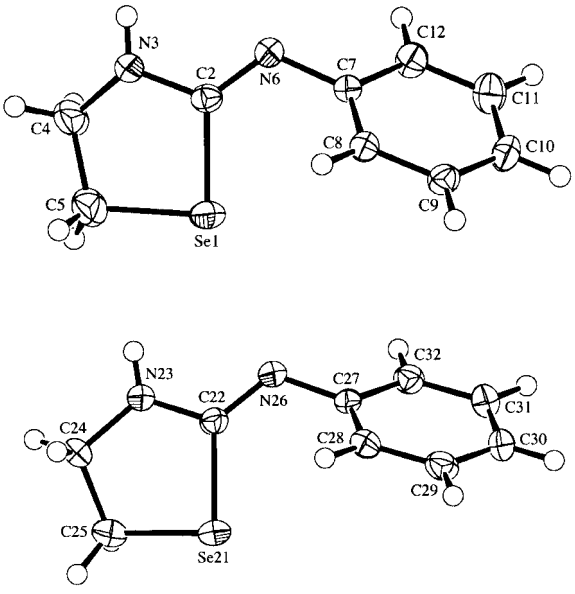


Figure 1. ORTEP plot[58] of the molecular structure of the two symmetry-independent molecules of **9a** (arbitrary numbering of atoms; displacement ellipsoids with 50% probability).

In the case of **9a** there are two symmetry-independent molecules, in which the orientations of the phenyl rings are quite different, in the asymmetric unit. The five-membered ring in molecule A has an envelope conformation with C(4) as the envelope flap. The heterocyclic ring in molecule B also has an envelope conformation, but is more distorted from ideal geometry than the ring in molecule A and a different ring atom – C(25) – forms the envelope flap. Although the compound is achiral, it crystallized in a noncentrosymmetric polar space group. The absolute structure was determined independently by the diffraction experiment. The NH group in molecule A forms an intermolecular hydrogen bond with the imine N-atom of a neighboring molecule B. In turn, molecule B has the same mode of hydrogen bonding with the original molecule A, the hydrogen bonds thereby linking one molecule A and one molecule B into a dimeric unit by forming a loop with a binary graph set motif[59] of $R_2^2(8)$.

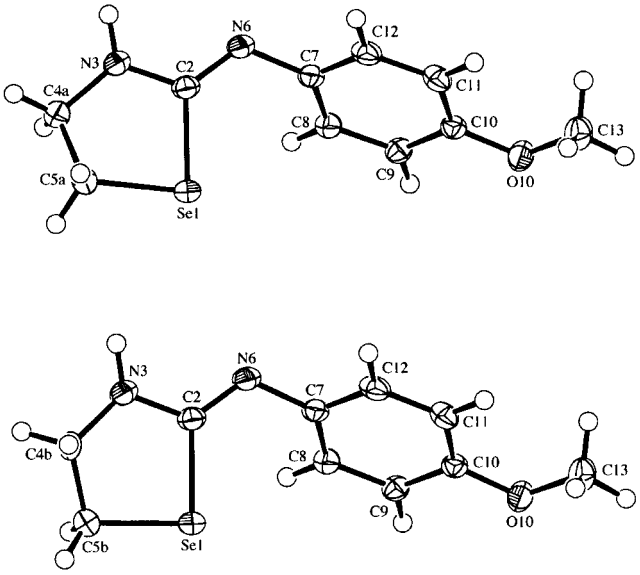


Figure 2. ORTEP plot[58] of the molecular structure of the two conformations of **9d** (arbitrary numbering of atoms; displacement ellipsoids with 50% probability).

In the case of **9d**, the methylene groups in the heterocyclic ring are disordered over two conformations, with the major conformation occurring in approximately 70% of the molecules. The heterocyclic ring in the major conformation has a slightly distorted half-chair conformation twisted on C(4a)–C(5a), with the distortion being in the direction of an envelope with C(5a) as the envelope flap. The minor conformation lies closer to that of an envelope with C(5b) as the envelope flap. The disorder is essentially the result of the envelope flap lying on opposite sides of the heterocyclic ring plane. Similarly to **9a**, the NH group forms an intermolecular hydrogen bond with the imine N-atom of a neighboring molecule. In turn, the acceptor molecule donates the same type of hydrogen bond back to the original molecule, thereby forming centrosymmetric dimeric units. The hydrogen bonding motif in these dimers is also $R_2^2(8)$.

The structures of the selenazan-2-imines **10** were similarly deduced from their elemental analyses and spectroscopic data. The molecular structures of **10a** and **10c** were verified by single-crystal X-ray analyses (Figure 3 and Figure 4).

There are two symmetry-independent molecules in the asymmetric unit of **10a**. The conformations of the independent molecules differ primarily in the puckering of the heterocyclic ring. In molecule A the ring has a screw-boat conformation, while in molecule B the ring has an envelope conformation with C(25) as the envelope flap. The NH group in molecule A forms an intermolecular hydrogen bond with the imine N-atom of a neighboring molecule A. In turn, the acceptor molecule donates the same type of

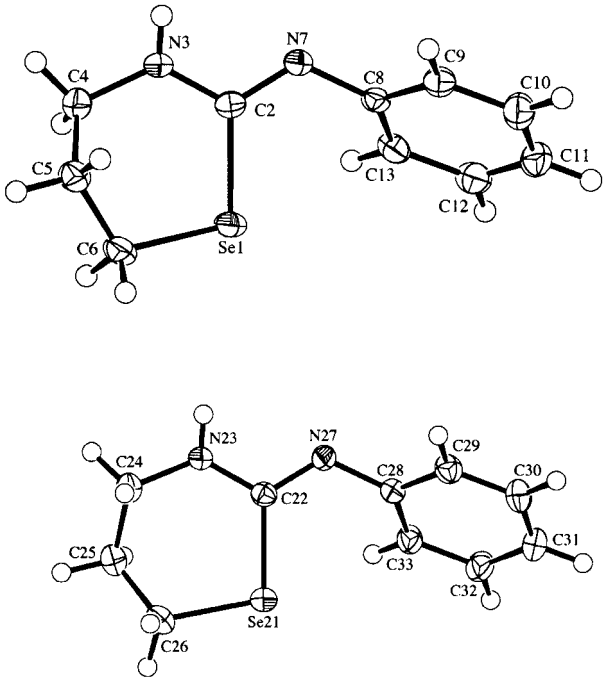


Figure 3. ORTEP plot[58] of the molecular structure of the two symmetry-independent molecules of **10a** (arbitrary numbering of atoms; displacement ellipsoids with 50% probability).

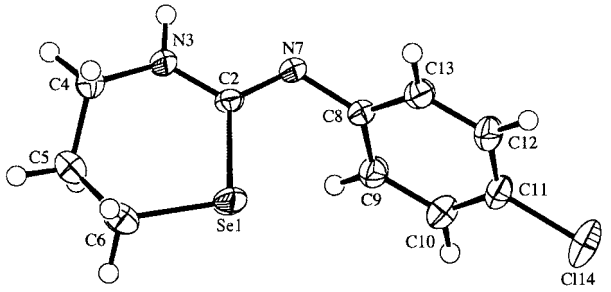
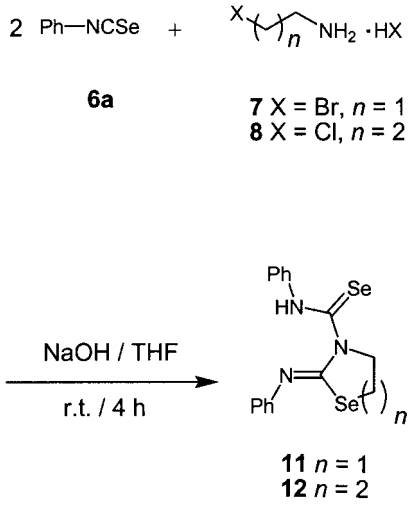


Figure 4. ORTEP plot[58] of the molecular structure of **10c** (arbitrary numbering of atoms; displacement ellipsoids with 50% probability).

hydrogen bond back to the original molecule, thereby forming centrosymmetric dimeric units composed entirely of A molecules. The hydrogen bonding motif[59] in these dimers is again $R_2^2(8)$. The same pattern of intermolecular hydrogen bonds links the B molecules into dimeric units.

In the case of **10c**, the heterocyclic ring has a distorted envelope conformation with C(5) as the envelope flap. The distortion is in the direction of a half-chair twisted on C(4)–C(5). Intermolecular hydrogen bonds between the NH group and the imine N-atom of a neighboring molecule link the molecules into centrosymmetric dimeric units, analogously to **10a**.

For the preparation of **9** and **10**, the organic base triethylamine was chosen to avoid secondary reactions. When stronger bases such as sodium hydroxide were used for the reactions of **6** with **7** and **8**, the formation of compounds **11** and **12**, respectively, was observed (Scheme 3). The 2:1 adduct **11** was obtained in 81% yield through a subsequent reaction between another equivalent of **6a** and the N-atom of the selenazolidine ring of **9a**. The homologous compound **12** was obtained similarly via the intermediate selenazane **10a**. In fact, the formation of product **11** was our first result in this study. We then focused our attention on the optimization of the synthesis of the initially formed selenazole ring by varying the solvent and the base. The optimal conditions proved to be a 1:1 mixture of **6** and **7** or **8** and two equivalents of triethylamine in dichloromethane at room temperature for ca. 4 h. The first equivalent of the base is needed to generate the free amine in situ, and the second to capture HX formed during the cyclization step. The triethylammonium salt was removed by washing the reaction mixture with water.



Scheme 3.

Crystallization of **11** from dichloromethane gave suitable crystals for the structure to be established by X-ray crystallography (Figure 5). Although the compound is achiral, it crystallized in a polar space group and the absolute structure was determined by the diffraction experiment. The five-membered heterocycle has an envelope conformation with C(5) as the envelope flap. The adjacent atoms N(6), C(7), C(13), and N(14) deviate only slightly from the plane defined by Se(1), C(2), N(3), and C(4), but the phenyl residues at N(6) and N(14) are twisted out of this plane by ca. 62° and 49°, respectively. The NH group forms an intramolecular hydrogen bond with the imine N-atom and thereby creates a six-membered loop with a graph set motif of S(6).

The above syntheses of 1,3-selenazolidines and 1,3-selenazanes are part of our research program started some years ago with the aim of synthesizing selenium-containing heterocycles. Notwithstanding, we also carried out a bibliographic search on the corresponding sulfur analogues: 1,3-thiazolidines and 1,3-thiazines. Surprisingly, we found no similar procedure for the preparation of these heterocycles from isothiocyanates and **7** or **8**, and so we decided to investigate these reactions too. Under analogous conditions we obtained the 1,3-thiazolidines **14a** and **14b** and the 1,3-thiazanes **15a** and **15b** in almost quantitative yields (Scheme 4, Table 2).

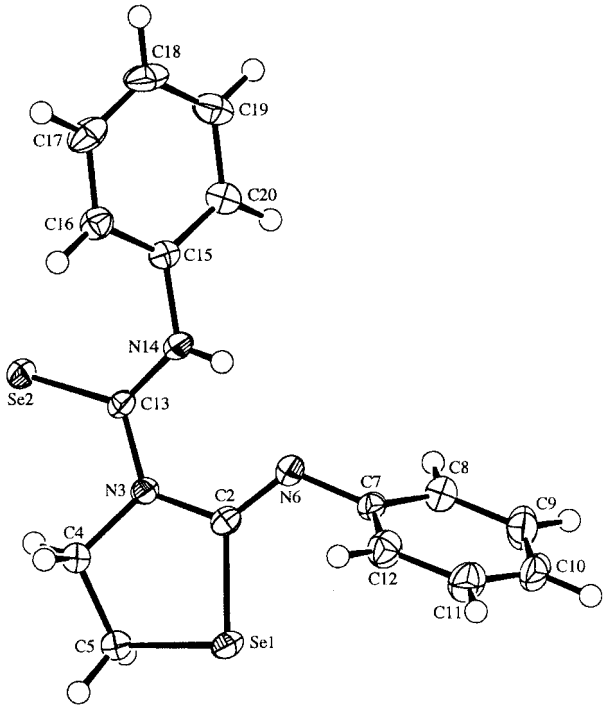
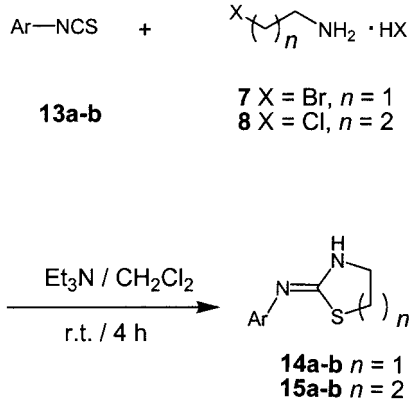


Figure 5. ORTEP plot[58] of the molecular structure of **11** (arbitrary numbering of atoms; displacement ellipsoids with 50% probability).



Scheme 4.

Conclusions

In summary, we have shown that 1,3-selenazolidin-2-imines **9** and 1,3-selenazin-2-imines **10** can easily be synthesized with excellent yields in one-pot reactions by starting from aryl and alkyl isoselenocyanates and ω-haloalkylamines in basic media. The analogous reaction with isothiocyanates opens a novel and efficient route to the corresponding sulfur heterocycles.

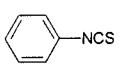
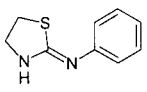
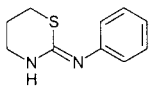
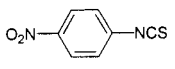
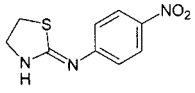
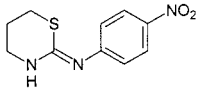
Experimental Section

General Remarks: TLC: silica gel 60 F_{254} plates (0.25 mm; Merck). Column chromatography (CC): silica gel 60 (0.040–0.063 mm; Merck). Melting point (M.p.): Büchi B-540 apparatus, in capillary; uncorrected. IR spectra: KBr (cm^{-1}).^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra: Bruker ARX 300 instrument, in $CDCl_3$ unless otherwise specified; chemical shifts in ppm, coupling constants (*J*) in Hz. EI-MS and CI-MS: Finnigan SSQ-700 or MAT-90 instruments. EI mode: 70 eV; CI mode: NH_3 as carrier gas.

Starting Materials: 2-Bromoethylamine (HBr salt) and 3-chloropropylamine (HCl salt) are commercially available (Fluka). Isoselenocyanates were prepared by Barton's procedure, by starting from formamides.[34a] Formanilide and *N*-cyclohexylformamide are commercially available (Fluka and Aldrich), *N*-(4-chlorophenyl)-, *N*-(4-bromophenyl)-, and *N*-(4-methoxyphenyl)formamide were prepared from the corresponding anilines and 95% formic acid by a slightly modified literature protocol:[60] the solution was heated to reflux for 30 min and the solvents were evaporated to dryness in vacuo. The residue was dissolved in Et_2O and washed with dilute AcOH (5%), H_2O, and aqueous $NaHCO_3$ (5% aq.). The aqueous layer was extracted with Et_2O, and the combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure. The crude products were purified by recrystallization from mixtures of EtOH and H_2O.

General Procedure for the Preparation of 1,3-Selenzolidines 9a–g and 1,3-Selenazanes 10a–g: A 25 mL round-bottomed flask fitted with a magnetic stirrer and condenser was charged with a solution of the appropriate isoselenocyanate (1.0 mmol) in CH_2Cl_2 (20 mL). 2-Bromoethylamine hydrobromide or 3-chloropropylamine hydrochloride (1.0 mmol) was added, followed by Et_3N (0.28 mL, 2.0 mmol), and the mixture was stirred for 4 h at room temperature (except for cyclohexyl isoselenocyanate: 12 h). The mixture was washed with H_2O (3 × 10 mL) and the solvents were evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on silica gel with hexane/AcOEt (1:0 to 1:1).

Table 2. Preparation of 1,3-thiazolidines **14** and 1,3-thiazines **15** from isothiocyanates **13**.

Entry	13	14	Yield (%)	15	Yield (%)
a			97		99
b			98		99

Phenyl(1,3-selenazolidin-2-yliden)amine (9a): Yield: 146 mg (65%). Colorless crystals. M.p. 167–169 °C (CH_2Cl_2). ^1H NMR: δ = 3.31 (t, J = 6.8 Hz, 2 H), 3.74 (t, J = 6.8 Hz, 2 H), 6.15 (br s, NH), 7.04–7.09 (m, 3 × arom. H), 7.28 (t, J = 6.2 Hz, 2 × arom. H) ppm. ^{13}C NMR: δ = 25.8 (CH_2), 49.5 (CH_2), 121.1 (2 × arom. CH), 123.5 (1 × arom. CH), 129.0 (2 × arom. CH), 149.7 (1 × arom. C), 160.1 (C(2)) ppm. IR: $\tilde{\nu}$ = 1630 (s), 1584 (s), 1488 (m), 1354 (w), 1291 (w), 1253 (w), 1194 (m), 1163 (w), 1074 (m), 943 (w), 900 (w), 836 (m), 769 (m), 700 (m) cm^{-1}. CI-MS: 225 (49) [M(^{78}Se) + H]$^+$, 227 (100) [M(^{80}Se) + H]$^+$. $C_9H_{10}N_2Se$ (225.15): C 48.01, H 4.48, N 12.44; found: C 48.17, H 4.52, N 12.43.

Suitable crystals for the X-ray crystal structure determination were grown from CH_2Cl_2 by slow evaporation of the solvent.

(4-Bromophenyl)(1,3-selenazolidin-2-yliden)amine (9b): Yield: 292 mg (96%). Yellowish crystals. M.p. 160–162 °C (CH_2Cl_2). ^1H NMR: δ = 3.33 (t, J = 6.8 Hz, CH_2), 3.70 (t, J = 6.8 Hz, CH_2), 6.90 (br s, NH), 6.90, 7.38 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 25.4 (CH_2), 48.5 (CH_2), 116.4 (1 × arom. C), 122.9 (2 × arom. CH), 132.0 (2 × arom. CH), 149.4 (1 × arom. C), 160.8 (C(2)) ppm. IR: $\tilde{\nu}$ = 1625 (s, br), 1575 (m), 1486 (m), 1458 (w), 1254 (w), 1197 (m), 1100 (w), 1071 (m), 841 (w) cm^{-1}. CI-MS: 303 (46) [M(^{78}Se, ^{79}Br) + H]$^+$, 304 (15), 305 (100) [M(^{80}Se, ^{79}Br) + H]$^+$, 306 (11), 307 (78) [M(^{80}Se, ^{81}Br) + H]$^+$. $C_9H_9N_2SeBr$ (304.05): C 35.55, H 3.31, N 9.21; found: C 35.65, H 3.16, N 9.05.

(4-Chlorophenyl)(1,3-selenazolidin-2-yliden)amine (9c): Yield: 220 mg (85%). Yellowish crystals. M.p. 162–164 °C (CH_2Cl_2). ^1H NMR: δ = 3.33 (t, J = 6.8 Hz, CH_2), 3.74 (t, J = 6.8 Hz, CH_2), 5.15 (br s, NH), 6.95, 7.25 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 25.5 (CH_2), 48.6 (CH_2), 122.5 (2 × arom. CH), 128.9 (1 × arom. C), 129.0 (2 × arom. CH), 148.5 (1 × arom. C), 161.0 (C(2)) ppm. IR: $\tilde{\nu}$ = 1625 (s, br), 1579 (m), 1488 (m), 1460 (w), 1354 (w), 1298 (w), 1254 (w), 1197 (m), 1073 (w), 833 (w) cm^{-1}. CI-MS: 259 (47) [M(^{78}Se, ^{35}Cl) + H]$^+$, 260 (10), 261 (100) [M(^{80}Se, ^{35}Cl) + H]$^+$, 263 (42) [M(^{80}Se, ^{37}Cl) + H]$^+$. $C_9H_9N_2SeCl$ (259.59): C 41.64, H 3.49, N 10.79; found: C 41.55, H 3.75, N 10.63.

(4-Methoxyphenyl)(1,3-selenazolidin-2-yliden)amine (9d): Yield: 166 mg (65%). Colorless crystals. M.p. 133–135 °C (CH_2Cl_2). ^1H NMR: δ = 3.27 (t, J = 6.8 Hz, CH_2), 3.71 (t, J = 6.8 Hz, CH_2), 3.78 (s, Me), 6.34 (br s, NH), 6.82, 6.96 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 25.6 (CH_2), 49.3 (CH_2), 55.3 (Me), 114.2 (2 × arom. CH), 122.4 (2 × arom. CH), 143.6 (1 × arom. C), 156.0 (1 × arom. C), 160.6 (C(2)) ppm. IR: $\tilde{\nu}$ = 1631 (s, br), 1504 (s), 1356 (w), 1293 (m), 1243 (s), 1192 (s), 1099 (w), 1068 (m), 1035 (m), 944 (w), 825 (m), 764 (m) cm^{-1}. CI-MS: 255 (51) [M(^{78}Se) + H]$^+$, 257 (100) [M(^{80}Se) + H]$^+$. $C_{10}H_{12}N_2OSe$ (255.18): C 47.07, H 4.74, N 10.98; found: C 46.73, H 4.73, N 10.77.

(4-Methylphenyl)(1,3-selenazolidin-2-yliden)amine (9e): Yield: 170 mg (71%). Colorless crystals. M.p. 142–144 °C (CH_2Cl_2). ^1H NMR: δ = 2.31 (s, Me), 3.32 (t, J = 6.8 Hz, CH_2), 3.75 (t, J = 6.8 Hz, CH_2), 6.02 (br s, NH), 6.95, 7.09 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 20.8 (Me), 25.9 (CH_2), 49.8 (CH_2), 121.0 (2 × arom. CH), 129.6 (2 × arom. CH), 133.1 (1 × arom. C), 146.9 (1 × arom. C), 159.9 (C(2)) ppm. IR: $\tilde{\nu}$ = 1630 (s), 1599 (s), 1505 (m), 1461 (w), 1351 (w), 1290 (w), 1252 (w), 1194 (m), 1172 (w), 1108 (w), 1071 (w), 820 (m), 772 (w) cm^{-1}. CI-MS: 239 (48) [M(^{78}Se) + H]$^+$, 241 (100) [M(^{80}Se) + H]$^+$. $C_{10}H_{12}N_2Se$ (239.18): C 50.22, H 5.06, N 11.71; found: C 50.52, H 5.23, N 11.76.

(2,6-Dimethylphenyl)(1,3-selenazolidin-2-yliden)amine (9f): Yield: 180 mg (71%). Colorless crystals. M.p. 142–144 °C (CH_2Cl_2). ^1H NMR: δ = 2.18 (s, 2 × Me), 3.25 (t, J = 6.8 Hz, CH_2), 3.63 (t, J = 6.8 Hz, CH_2), 6.15 (br s, NH), 6.88–6.98 (m, 1 × arom. H), 7.38 (d, J = 8.7 Hz, 2 × arom. H) ppm. ^{13}C NMR: δ = 18.0 (2 × Me), 24.9 (CH_2), 48.2 (CH_2), 123.7 (2 × arom. C), 127.9 (2 × arom. CH), 130.5 (2 × arom. C), 149.0 (1 × arom. C), 161.4 (C(2)) ppm. IR: $\tilde{\nu}$ = 1636 (s, br), 1588 (m), 1472 (m), 1431 (w), 1352 (w), 1286 (w), 1258 (w), 1191 (w), 1091 (w), 834 (w), 766 (m) cm^{-1}. CI-MS: 253 (56) [M(^{78}Se) + H]$^+$, 255 (100) [M(^{80}Se) + H]$^+$. $C_{11}H_{14}N_2Se$ (253.20): C 52.18, H 5.57, N 11.06; found: C 52.32, H 5.33, N 11.36.

(Cyclohexyl)(1,3-selenazolidin-2-yliden)amine (9g): Yield: 90 mg (39%). Yellowish crystals. M.p. 173–175 °C (CH_2Cl_2) (ref.[74] 170°). ^1H NMR: δ = 1.29–1.54 (m, 4 H), 1.56–1.83 (m, 4 H), 2.01–2.07 (m, 2 H), 3.18 (t, J = 6.8, Hz CH_2), 4.42–4.50 (m, 1 H), 5.08 (t, J = 6.8 Hz, CH_2), 5.85 (br s, NH) ppm. ^{13}C NMR: δ = 19.2 (CH_2), 24.1 (2 × CH_2), 25.4 (CH_2), 33.5 (2 × CH_2), 56.6 (CH_2), 58.9 (CH), 151.1 (C(2)) ppm. IR: $\tilde{\nu}$ = 1726 (w), 1668 (m), 1567 (s, br), 1449 (m), 1410 (w), 1362 (w), 1307 (w), 1277 (w), 1223 (w), 1159 (m), 1137 (w), 1073 (w), 1025 (w), 975 (w), 890 (w), 854 (m), 794 (w), 736 (w) cm^{-1}. CI-MS: 231 (48) [M(^{78}Se) + H]$^+$, 233 (100) [M(^{80}Se) + H]$^+$. $C_9H_{16}N_2Se$ (231.20): C 46.76, H 6.98, N 12.12; found: C 46.66, H 6.46, N 11.85.

Phenyl(1,3-selenazan-2-yliden)amine (10a): Yield: 210 mg (88%). Yellowish crystals. M.p. 121–123 °C (CH_2Cl_2). ^1H NMR: δ = 2.04–2.11 (m, CH_2), 3.01 (t, J = 6.8 Hz, CH_2), 3.41 (t, J = 6.8 Hz, CH_2), 5.74 (br s, 1 H), 7.02–7.07 (m, 3 × arom. H), 7.23–7.29 (m, 2 × arom. H) ppm. ^{13}C NMR: 20.9 (CH_2), 23.9 (CH_2), 44.7 (CH_2), 122.3 (2 × arom. CH), 123.5 (1 × arom. CH), 128.9 (2 × arom. CH), 146.5 (1 × arom. C), 149.6 (C(2)) ppm. IR: $\tilde{\nu}$ = 1630 (s), 1584 (s), 1488 (m), 1354 (w), 1291 (w), 1253 (w), 1194 (m), 1163 (w), 1074 (m), 943 (w), 900 (w), 836 (m), 769 (m), 700 (m) cm^{-1}. CI-MS: 239 (50) [M(^{78}Se) + H]$^+$, 241 (100) [M(^{80}Se) + H]$^+$. $C_{10}H_{12}N_2Se$ (239.18): C 50.22, H 6.06, N 11.71; found: C 50.66, H 5.23, N 11.76.

Suitable crystals for the X-ray crystal-structure determination were grown from CH_2Cl_2 by slow evaporation of the solvent.

(4-Bromophenyl)(1,3-selenazan-2-yliden)amine (10b): Yield: 299 mg (94%). M.p. 141–143 °C (CH_2Cl_2). ^1H NMR: δ = 2.05–2.13 (m, CH_2), 3.00 (t, J = 6.8 Hz, CH_2), 3.39 (t, J = 6.8 Hz, CH_2), 6.02 (br s, NH), 6.89, 7.35 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 20.8 (CH_2), 24.0 (CH_2), 44.3 (CH_2), 115.9 (1 × arom. C), 123.9 (2 × arom. CH), 131.8 (2 × arom. CH), 146.5 (1 × arom. C), 149.6 (C(2)) ppm. IR: $\tilde{\nu}$ = 1621 (s, br), 1575 (s), 1488 (s), 1463 (m), 1427 (w), 1385 (w), 1349 (w), 1319 (w), 1276 (w), 1265 (w), 1203 (s), 1159 (s), 1098 (m), 1066 (w), 1003 (m), 944 (w), 869 (w), 833 (m), 754 (w) cm^{-1}. CI-MS: 317 (100) [M(^{78}Se, ^{79}Br) + H]$^+$, 318 (17), 319 (100) [M(^{80}Se, ^{79}Br) + H]$^+$, 321 (77) [M(^{80}Se, ^{81}Br) + H]$^+$. $C_{10}H_{11}N_2SeBr$ (318.07): C 37.76, H 3.49, N 8.81; found: C 37.84, H 3.60, N 8.81.

(4-Chlorophenyl)(1,3-selenazan-2-yliden)amine (10c): Yield: 216 mg (79%). Yellowish crystals. M.p. 134–136 °C (CH_2Cl_2). ^1H NMR: δ = 2.08–2.17 (m, CH_2), 3.02 (t, J = 6.8 Hz, CH_2), 3.42 (t, J = 6.8 Hz, CH_2), 5.20 (br s, NH), 6.96, 7.23 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 20.8 (CH_2), 24.0 (CH_2), 44.3 (CH_2), 123.5 (2 × arom. CH), 128.2 (1 × arom. C), 128.8 (2 × arom. CH), 146.2 (1 × arom. C), 149.8 (C(2)) ppm. IR: $\tilde{\nu}$ = 1625 (s), 1583 (m), 1489 (s), 1463 (m), 1428 (w), 1384 (w), 1351 (w), 1320 (w), 1269 (w), 1207 (s), 1159 (s), 1103 (m), 1086 (m), 1010 (m), 870 (m), 837 (m), 765 (w) cm^{-1}. CI-MS: 273 (50) [M(^{78}Se, ^{35}Cl) + H]$^+$, 274 (12), 275 (100) [M(^{80}Se, ^{35}Cl) + H]$^+$, 277 (44) [M(^{80}Se, ^{37}Cl) + H]$^+$. $C_{10}H_{11}N_2SeCl$ (273.62): C 43.90, H 4.05, N 10.24; found: C 44.13, H 4.24, N 10.17.

Suitable crystals for the X-ray crystal structure determination were grown from CH_2Cl_2 by slow evaporation of the solvent.

(4-Methoxyphenyl)(1,3-selenazan-2-yliden)amine (10d): Yield: 247 mg (92%). Yellowish crystals. M.p. 113–115 °C (CH_2Cl_2). ^1H

NMR: δ = 2.04–2.12 (m, CH_2), 2.98 (t, J = 6.8 Hz, CH_2), 3.39 (t, J = 6.8 Hz, CH_2), 3.78 (s, Me), 6.12 (br s, NH), 6.81, 6.95 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 20.7 (CH_2), 24.0 (CH_2), 44.5 (CH_2), 55.3 (Me), 114.0 (2 × arom. CH), 123.6 (2 × arom. CH), 139.9 (1 × arom. C), 149.9 (1 × arom. C), 156.0 (C(2)) ppm. IR: $\tilde{\nu}$ = 1632 (s, br), 1504 (s), 1459 (m), 1439 (w), 1346 (m), 1316 (w), 1235 (s), 1206 (s), 1162 (m), 1099 (m), 1033 (s), 1015 (m), 949 (w), 871 (m), 839 (m), 758 (m), 726 (w) cm^{-1}. CI-MS: 269 (51) [M(^{78}Se) + H]$^+$, 271 (100) [M(^{80}Se) + H]$^+$. $C_{11}H_{14}N_2OSe$ (269.21): C 49.08, H 5.24, N 10.41; found: C 49.24, H 5.41, N 10.35.

(4-Methylphenyl)(1,3-selenazan-2-yliden)amine (10e): Yield: 220 mg (87%). Yellowish crystals. M.p. 107–109 °C (CH_2Cl_2). ^{1}H NMR: δ = 2.03–2.11 (m, CH_2), 2.30 (s, Me), 2.99 (t, J = 6.8 Hz, CH_2), 3.40 (t, J = 6.8 Hz, CH_2), 5.65 (br s, NH), 6.93, 7.07 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: δ = 20.8 (Me, CH_2), 23.8 (CH_2), 44.6 (CH_2), 122.3 (2 × arom. CH), 129.4 (2 × arom. CH), 133.0 (1 × arom. C), 143.6 (1 × arom. C), 149.9 (C(2)) ppm. IR: $\tilde{\nu}$ = 1622 (s), 1602 (s), 1506 (s), 1470 (m), 1427 (w), 1377 (w), 1349 (m), 1313 (m), 1265 (m), 1212 (m), 1161 (m), 1101 (w), 1011 (w), 945 (w), 873 (m), 822 (m), 761 (w), 717 (w) cm^{-1}. CI-MS: 253 (53) [M(^{78}Se) + H]$^+$, 255 (100) [M(^{80}Se) + H]$^+$. $C_{11}H_{14}N_2Se$ (253.20): C 52.18, H 5.57, N 11.06; found: C 52.43, H 5.79, N 11.33.

(2,6-Dimethylphenyl)(1,3-selenazan-2-yliden)amine (10f): Yield: 235 mg (88%). Yellowish crystals. M.p. 133–135 °C (CH_2Cl_2). ^{1}H NMR: δ = 2.04–2.12 (m, CH_2), 2.18 (s, 2 × Me), 2.91 (t, J = 6.8 Hz, CH_2), 3.30 (t, J = 6.8 Hz, CH_2), 6.02 (br s, NH), 6.87–7.00 (m, 3 × arom. H) ppm. ^{13}C NMR: δ = 18.1 (2 × Me), 20.2 (CH_2), 24.7 (CH_2), 43.8 (CH_2), 123.3 (1 × arom. CH), 127.7 (2 × arom. CH), 131.1 (2 × arom. C), 145.4 (1 × arom. C), 149.5 (C(2)) ppm. IR: $\tilde{\nu}$ = 1615 (s), 1584 (s), 1506 (w), 1480 (s), 1432 (m), 1383 (w), 1351 (w), 1313 (s), 1265 (s), 1252 (m), 1202 (s), 1163 (s), 1105 (m), 1090 (s), 1004 (m), 872 (m), 828 (m), 778 (m), 764 (s), 703 (w) cm^{-1}. CI-MS: 267 (54) [M(^{78}Se) + H]$^+$ 269 (100) [M(^{80}Se) + H]$^+$. $C_{12}H_{16}N_2Se$ (267.23): C 53.93, H 6.04, N 10.48; found: C 54.04, H 6.30, N 10.23.

Cyclohexyl(1,3-selenazan-2-yliden)amine (10g): Yield: 225 mg (92%). Colorless crystals. M.p. 113–115 °C (CH_2Cl_2). ^{1}H NMR: δ = 1.08–1.29 (m, 4 H), 1.32–1.41 (m, 2 H), 1.66–1.81 (m, 4 H), 1.94–2.01 (m, 2 H), 3.10 (t, J = 6.8 Hz, CH_2), 3.50 (t, J = 6.8 Hz, CH_2), 3.58–3.67 (m, 1 H), 4.45 (br s, NH) ppm. ^{13}C NMR: δ = 20.9 (CH_2), 21.3 (CH_2), 24.7 (2 × CH_2), 25.7 (CH_2), 33.3 (2 × CH_2), 47.7 (CH_2), 51.1 (CH), 145.6 (C(2)) ppm. IR: $\tilde{\nu}$ = 1609 (s, br), 1525 (s), 1448 (m), 1374 (m), 1339 (m), 1295 (w), 1282 (w), 1258 (w), 1240 (m), 1169 (w), 1150 (m), 1099 (m), 1062 (w), 1002 (w), 972 (m), 925 (w), 889 (w), 859 (w), 826 (w), 730 (w) cm^{-1}. CI-MS: 245 (48) [M(^{78}Se) + H]$^+$, 247 (100) [M(^{80}Se) + H]$^+$. $C_{10}H_{18}N_2Se$ (245.22): C 48.98, H 7.40, N 11.42; found: C 49.16, H 7.23, N 11.02.

General Procedure for the Preparation of 11 and 12: A 25 mL round-bottomed flask fitted with a magnetic stirrer and condenser was charged with a solution of the phenyl isoselenocyanate (1.0 mmol) in THF (20 mL). Bromoethylamine hydrobromide (for **11**) or 3-chloropropylamine hydrochloride (for **12**) (0.5 equiv.) was added, followed by aqueous NaOH (1 M, 2 equiv.), and the mixture was stirred for 6 h at room temperature. The mixture was then diluted with CH_2Cl_2 (50 mL), washed with H_2O (3 × 15 mL), and dried over $MgSO_4$, and the solvents were evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on silica gel with hexane/AcOEt (3:1 to 1:3).

2-(Phenylimino)-1,3-selenazolidine-3-carboselenoic Anilide (11): Yield: 173 mg (81%). Yellowish crystals. M.p. 119–121 °C (CH_2Cl_2). ^{1}H NMR: 3.21 δ = (t, J = 6.8 Hz, CH_2), 5.29 (t, J = 6.8 Hz, CH_2), 6.96 (d, J = 8.2 Hz, 2 × arom. H), 7.19–7.41 (m, 6 × arom. H), 7.51 (d, J = 8.2 Hz, 2 × arom. H) ppm. ^{13}C NMR: δ = 18.9 (CH_2), 60.2 (CH_2), 120.6 (2 × arom. CH), 125.7 (1 × arom. CH), 126.0 (2 × arom. CH), 127.0 (1 × arom. CH), 128.8 (2 × arom. CH), 129.4 (2 × arom. CH), 139.8, 149.6 (2 × arom. C), 156.9 (C(2)), 180.4 (C=Se) ppm. IR: $\tilde{\nu}$ = 1586 (s), 1540 (s), 1486 (m), 1382 (w), 1288 (m), 1249 (w), 1216 (m), 1164 (s), 1152 (m), 1069 (w), 1053 (w), 867 (w), 761 (w), 738 (w), 694 (m) cm^{-1}. CI-MS: 227 (100), 407 (2) [M(^{78}Se) + H]$^+$, 409 (5) [M(^{80}Se) + H]$^+$. $C_{16}H_{15}N_3Se_2$ (407.24): C 47.19, H 3.71, N 10.32; found: C 47.05, H 3.59, N 10.08.

Suitable crystals for the X-ray crystal structure determination were grown from CH_2Cl_2 by slow evaporation of the solvent.

2-(Phenylimino)-1,3-selenazane-3-carboselenoic Anilide (12): Yield: 345 mg (82%). Orange crystals. M.p. 160–162 °C (CH_2Cl_2). ^{1}H NMR: δ = 2.37 (quint, J = 6.8 Hz, CH_2), 3.08 (t, J = 6.8 Hz, CH_2), 4.42 (t, J = 8.1 Hz, CH_2), 6.95 (d, J = 7.3 Hz, 4 × arom. H), 7.16 (t, J = 7.4 Hz, 2 × arom. H), 7.28–7.37 (m, 4 × arom. H) ppm. ^{13}C NMR: δ = 27.2 (CH_2), 28.1 (CH_2), 50.7 (CH_2), 120.7 (1 × arom. CH), 120.9 (2 × arom. CH), 125.1 (2 × arom. CH), 129.3 (1 × arom. CH), 129.5 (4 × arom. CH), 146.8 (1 × arom. C), 149.9 (1 × arom. C), 151.0 (C(2)), 178.2 (C=Se) ppm. IR: $\tilde{\nu}$ = 1661 (w), 1606 (s), 1575 (s), 1485 (w), 1420 (w), 1374 (w), 1263 (m), 1239 (w), 1193 (w), 1116 (w), 1023 (w), 902 (w), 844 (w), 762 (s), 694 (s) cm^{-1}. CI-MS: 240 (68), 420 (45) [M(^{78}Se,^{78}Se) + H]$^+$, 422 (22) [M(^{78}Se,^{80}Se) + H]$^+$, 424 (100, [M(^{80}Se,^{80}Se) + H]$^+$. $C_{17}H_{17}N_3Se_2$ (421.26): C 48.47, H 4.07, N 9.97; found: C 48.35, H 3.97, N 10.12.

General Procedure for the Preparation of 1,3-Thiazolidines 14 and 1,3-Thiazines 15: A 25 mL round-bottomed flask fitted with a magnetic stirrer and condenser was charged with a solution of the appropriate isothiocyanate (1.0 mmol) in CH_2Cl_2 (20 mL). 2-Bromoethylamine hydrobromide (**7**) or 3-chloropropylamine hydrochloride (**8**; 1.0 mmol) was added, followed by triethylamine (0.28 mL, 2.0 mmol) and the mixture was stirred for 4 h at room temperature. The mixture was then washed with H_2O (3 × 10 mL) and dried over $MgSO_4$, and the solvents were evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on silica gel with hexane/AcOEt (1:0 to 1:1).

Phenyl(1,3-thiazolidin-2-yliden)amine (14a): Yield: 173 mg (97%). White crystals. M.p. 159–161 °C (CH_2Cl_2). ^{1}H NMR: δ = 3.28 (t, J = 7.0 Hz, CH_2), 3.80 (t, J = 7.0 Hz, CH_2), 5.29 (br s, 1 H), 7.03 (t, J = 7.1 Hz, 1 × arom. H), 7.12 (d, J = 7.4 Hz, 2 × arom. H), 7.28 (t, J = 7.3 Hz, 2 × arom. H) ppm. ^{13}C NMR: δ = 31.9 (CH_2), 50.7 (CH_2), 121.0 (2 × arom. CH), 123.1 (1 × arom. CH), 128.8 (2 × arom. CH), 147.3 (1 × arom. C), 161.5 (C(2)) ppm. IR: $\tilde{\nu}$ = 1626 (s), 1586 (s), 1490 (m), 1351 (w), 1296 (w), 1204 (m), 1185 (w), 1169 (w), 1154 (w), 1074 (m), 950 (w), 901 (w), 844 (w), 767 (m), 694 (m) cm^{-1}. CI-MS: 179 (100) [M + H]$^+$, 180 (11). $C_9H_{10}N_2S$ (178.26): C 60.64, H 5.65, N 15.72; found: C 60.49, H 5.52, N 15.44.

(4-Nitrophenyl)(1,3-thiazolidin-2-yliden)amine (14b): Yield: 219 mg (98%). White crystals. M.p. 157–159 °C (CH_2Cl_2). ^{1}H NMR: δ = 3.30 (t, J = 7.0 Hz, CH_2), 3.76 (t, J = 7.0 Hz, CH_2), 5.40 (br s, 1 H), 6.97, 7.38 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: 31.5 (CH_2), 49.2 (CH_2), 122.9 (2 × arom. CH), 131.8 (2 × arom. CH), 147.3 (1 × arom. C), 155.8 (1 × arom. C), 161.9 (C(2)) ppm. IR: $\tilde{\nu}$ = 1627 (s, br), 1575 (s), 1486 (s), 1459 (m), 1435 (w), 1356 (w), 1301 (w), 1258 (w), 1222 (w), 1206 (m), 1185 (w), 1170 (w), 1101 (w), 1072 (m), 1002 (w), 887 (w), 849 (w), 831 (w), 775 (w) cm^{-1}. CI-MS: 224 (100) [M + H]$^+$, 225 (15). $C_9H_9N_3O_2S$ (223.26): C 48.42, H 4.06, N 18.82, S 14.36; found: C 48.48, H 3.85, N 18.79, S 14.67.

Phenyl(1,3-thiazan-2-yliden)amine (15a): Yield: 190 mg (99%). White crystals. M.p. 124–125 °C (CH_2Cl_2). ^{1}H NMR: δ = 1.97–

2.05 (m, CH_2), 2.99 (t, J = 6.0 Hz, CH_2), 3.46 (t, J = 5.7 Hz, CH_2), 5.47 (br s, 1 H), 7.00 (t, J = 7.2 Hz, 1 × arom. H), 7.07 (d, J = 7.3 Hz, 2 × arom. H), 7.26 (t, J = 7.4 Hz, 2 × arom. H) ppm. ^{13}C NMR: δ = 22.5 (CH_2), 27.0 (CH_2), 43.1 (CH_2), 122.0 (2 × arom. CH), 122.7 (1 × arom. CH), 128.7 (2 × arom. CH), 146.1 (1 × arom. C), 151.7 (C(2)) ppm. IR: $\tilde{\nu}$ = 1612 (s), 1580 (s), 1492 (s), 1460 (m), 1383 (w), 1347 (w), 1321 (m), 1268 (w), 1217 (m), 1171 (w), 1162 (m), 1102 (w), 1070 (w), 1016 (m), 904 (w), 880 (w), 770 (m), 702 (m) cm^{-1}. CI-MS: 193 (100) $[M + H]^+$, 194 (12). $C_{10}H_{12}N_2S$ (192.28): C 62.46, H 6.29, N 14.57; found: C 62.34, H 6.11, N 14.57.

(4-Nitrophenyl)(1,3-thiazan-2-yliden)amine (15b): Yield: 234 mg (99%). White crystals. M.p. 156–158 °C (CH_2Cl_2). ^{1}H NMR: δ = 2.04 (m, CH_2), 2.99 (t, J = 6.1 Hz, CH_2), 3.44 (t, J = 5.7 Hz, CH_2), 5.17 (br s, 1 H), 6.92, 7.35 (AA′BB′, 4 × arom. H) ppm. ^{13}C NMR: 22.5 (CH_2), 26.9 (CH_2), 43.0 (CH_2), 123.7 (2 × arom. CH), 131.7 (2 × arom. CH), 145.4 (1 × arom. C), 155.4 (1 × arom. C), 162.4 (C(2) ppm. IR: $\tilde{\nu}$ = 1624 (s), 1575 (s), 1487 (s), 1463 (m), 1436 (w), 1390 (w), 1352 (w), 1271 (w), 1211 (s), 1171 (w), 1160 (s), 1109 (m), 1064 (w), 1005 (w), 880 (w), 838 (m), 770 (w), 663 (m) cm^{-1}. CI-MS: 238 (100) $[M + H]^+$, 239 (13). $C_{10}H_{11}N_3O_2S$ (237.28): C 50.62, H 4.67, N 17.71, S 13.51; found: C 50.32, H 4.67, N 17.89, S 13.29.

X-ray Crystal Structure Determinations of 9a, 9d, 10a, 10c, and 11 (Figures 1–5):[61] All measurements were performed on a Nonius KappaCCD area-detector diffractometer[62] with use of graphite-monochromated Mo-K_α radiation (λ, 0.71073 Å) and an Oxford Cryosystems Cryostream 700 cooler. The data collection and refinement parameters are given below, and views of the molecules are shown in Figure 1, Figure 2, Figure 3, Figure 4, and Figure 5. Data reduction was performed with HKL Denzo and Scalepack.[63] The intensities were corrected for Lorentz and polarization effects, and absorption corrections based on the multi-scan method[64] were applied. The structures were solved by direct methods by use of SIR92,[65] which revealed the positions of all non-H-atoms. In **9a** and **10a**, there are two symmetry-independent molecules in the asymmetric unit. In each case the atomic coordinates of the two molecules were tested carefully for a relationship from a higher symmetry space group by use of the PLATON program,[66] but none could be found. In **9d** the methylene groups of the heterocyclic ring are disordered over two conformations. Two sets of overlapping positions were defined for the atoms of these methylene groups, and the site occupation factor of the major conformation was refined to 0.697(8). Similarity restraints were applied to the chemically equivalent bond lengths and angles involving all disordered C-atoms, while neighboring disordered atoms within and between each conformation were restrained to have similar atomic displacement parameters.

For each structure, the non-H-atoms were refined anisotropically. The amine H-atoms were placed in the positions indicated by a difference electron density map and their positions were allowed to refine together with individual isotropic displacement parameters. All remaining H-atoms were placed in geometrically calculated positions and refined with the aid of a riding model in which each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for the methyl group of **9d**). The refinement of each structure was carried out on F^2 by full-matrix, least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in all cases. Refinement of the absolute structure parameter[67] for **9a** and **11** yielded a value of –0.02(1) in each case, which confidently confirms that the refined models represent the true absolute structures. In the case of **10a**, one reflection, the intensity of which was considered to be an extreme outlier, was omitted from the final refinement. Neutral atom scattering factors for non-H-atoms were taken from ref.[68], and the scattering factors for H-atoms were taken from ref.[69] Anomalous dispersion effects were included in F_c;[70] the values for f' and f'' were those of ref.[71] The values of the mass attenuation coefficients are those of ref.[72] All calculations were performed by use of the SHELXL97[73] program.

Crystal Data for 9a: $C_9H_{10}N_2Se$, M = 225.09, colorless, prism, crystal dimensions 0.07 × 0.17 × 0.22 mm^3, monoclinic, space group $P2_1$, Z = 4, a = 10.2191(3) Å, b = 7.4291(2) Å, c = 12.5009(3) Å, β = 109.531(1)°, V = 894.44(4) Å^3, D_X = 1.671 g·cm^{-3}, μ(Mo-K_α) = 4.138 mm^{-1}, T = 160 K, φ and ω scans, transmission factors (min.; max.) 0.531; 0.750, $2\theta_{max.}$ = 55°, total reflections measured 19758, symmetry independent reflections 4011, reflections with $I > 2\sigma(I)$ 3757, reflections used in refinement 4011, parameters refined 226, restraints 1, R (on F; $I > 2\sigma(I)$ reflections) = 0.0290, $wR(F^2)$ (all reflections) = 0.0692 ($w = (\sigma^2(F_o^2) + (0.0335P)^2 + 0.4923P)^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.047, secondary extinction coefficient 0.0096(9), final $\Delta_{max.}/\sigma$ 0.001, $\Delta\rho$ (max.; min.) = 0.52; –0.50 e·Å^{-3}.

Crystal Data for 9d: $C_{10}H_{12}N_2OSe$, M = 255.12, colorless, tablet, crystal dimensions 0.07 × 0.25 × 0.32 mm^3, monoclinic, space group $P2_1/c$, Z = 4, a = 6.2200(1), b = 11.0063(2), c = 15.0659(3) Å, β = 97.429(1)°, V = 1022.74(3) Å^3, D_X = 1.657 g·cm^{-3}, μ(Mo-K_α) = 3.637 mm^{-1}, T = 160 K, φ and ω scans, transmission factors (min.; max.) 0.496; 0.785, $2\theta_{max.}$ = 60°, total reflections measured 28650, symmetry independent reflections 2987, reflections with $I > 2\sigma(I)$ 2557, reflections used in refinement 2987, parameters refined 152, restraints 39, R (on F; $I > 2\sigma(I)$ reflections) = 0.0274, $wR(F^2)$ (all reflections) = 0.0699 ($w = (\sigma^2(F_o^2) + (0.037P)^2 + 0.3617P)^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.048, secondary extinction coefficient 0.007(1), final $\Delta_{max.}/\sigma$ 0.003, $\Delta\rho$ (max.; min.) = 0.65; –0.67 e·Å^{-3}.

Crystal Data for 10a: $C_{10}H_{12}N_2Se$, M = 239.12, pale yellow, prism, crystal dimensions 0.15 × 0.25 × 0.25 mm^3, monoclinic, space group $P2_1/n$, Z = 8, a = 14.4289(3), b = 10.0607(1), c = 15.1617(3) Å, β = 114.4143(9)°, V = 2004.14(6) Å^3, D_X = 1.585 g·cm^{-3}, μ(Mo-K_α) = 3.699 mm^{-1}, T = 160 K, φ and ω scans, transmission factors (min.; max.) 0.420; 0.585, $2\theta_{max.}$ = 55°, total reflections measured 47957, symmetry independent reflections 4599, reflections with $I > 2\sigma(I)$ 3914, reflections used in refinement 4598, parameters refined 244, R (on F; $I > 2\sigma(I)$ reflections) = 0.0296, $wR(F^2)$ (all reflections) = 0.0732 ($w = (\sigma^2(F_o^2) + (0.0341P)^2 + 1.3658P)^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.059, secondary extinction coefficient 0.0031(3), final $\Delta_{max.}/\sigma$ 0.001, $\Delta\rho$ (max.; min.) = 0.57; –0.84 e·Å^{-3}.

Crystal Data for 10c: $C_{10}H_{11}ClN_2Se$, M = 273.56, pale yellow, plate, crystal dimensions 0.05 × 0.27 × 0.30 mm^3, monoclinic, space group $P2_1/n$, Z = 4, a = 5.8994(1), b = 9.6760(2), c = 19.7407(3) Å, β = 95.085(1)°, V = 1122.42(3) Å^3, D_X = 1.619 g·cm^{-3}, μ(Mo-K_α) = 3.543 mm^{-1}, T = 160 K, φ and ω scans, transmission factors (min.; max.) 0.475; 0.844, $2\theta_{max.}$ = 60°, total reflections measured 28927, symmetry independent reflections 3268, reflections with $I > 2\sigma(I)$ 2889, reflections used in refinement 3268, parameters refined 132, R (on F; $I > 2\sigma(I)$ reflections) = 0.0293, $wR(F^2)$ (all reflections) = 0.0790 ($w = (\sigma^2(F_o^2) + (0.0401P)^2 + 0.5388P)^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.044, secondary extinction coefficient 0.007(1), final $\Delta_{max.}/\sigma$ 0.002, $\Delta\rho$ (max.; min.) = 0.45; –0.65 e·Å^{-3}.

Crystal Data for 11: $C_{16}H_{15}N_3Se_2$, M = 407.11, yellow, prism, crystal dimensions 0.10 × 0.22 × 0.25 mm^3, monoclinic, space group $P2_1$, Z = 2, a = 6.0296(1), b = 10.4131(3), c = 12.6809(3) Å, β

= 100.579(2)°, V = 782.66(3) Å^3, D_X = 1.727 g·cm^{-3}, μ(Mo-K_α) = 4.718 mm^{-1}, T = 160 K, φ and ω scans, transmission factors (min.; max.) 0.302; 0.635, $2\theta_{max.}$ = 60°, total reflections measured 20797, symmetry independent reflections 4553, reflections with $I > 2\sigma(I)$ 4186, reflections used in refinement 4553, parameters refined 195, restraints 1, R (on F; $I > 2\sigma(I)$ reflections) = 0.0308, $wR(F^2)$ (all reflections) = 0.0727 ($w = (\sigma^2(F_o^2) + (0.0359P)^2 + 0.3914P)^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.042, secondary extinction coefficient 0.006(1), final Δ_{max}/σ 0.001, $\Delta\rho$ (max.; min.) = 0.63; –0.78 e·Å^{-3}.

Acknowledgments

We thank the analytical services of our institute for NMR and mass spectra and for elemental analyses, Mr. B. Bürgi for his assistance with the determination of the crystal structures, and the Dr. Helmut Legerlotz-Foundation and F. Hoffmann–La Roche AG, Basel, for financial support.

[1] C. Paulmier, *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon Press, Oxford, **1986**.
[2] M. Renson, *The Chemistry of Organic Selenium and Tellurium Compounds*, vol. 1 (Eds.: S. Patai, Z. Rappoport), J. Wiley & Sons, New York, **1986**.
[3] A. Krief, L. Hevesi, *Organoselenium Chemistry I*, Springer Verlag, Berlin, Heidelberg, **1988**.
[4] T. Wirth, *Tetrahedron* **1999**, *55*, 1–28.
[5] V. P. Litvinov, V. D. Dyachenko, *Russ. Chem. Rev.* **1997**, *66*, 923–951.
[6] D. L. Klayman, W. H. H. Günther, *Organic Selenium Compounds: Their Chemistry and Biology*, John Wiley & Sons, New York, **1973**.
[7] *Topics in Current Chemistry: Organoselenium Chemistry, Modern Development in Organic Synthesis* (Ed.: T. Wirth), Springer Verlag, Berlin, **2000**, vol. 208.
[8] *Organoselenium Chemistry, A Practical Approach* (Ed.: T. G. Back), Oxford University Press, Oxford, **1999**.
[9] *Selenium in Biology and Medicine* (Ed.: A. Wengel), Springer Verlag, Berlin, **1989**.
[10] R. F. Burk, *Selenium in Biology and Human Health*, Springer Verlag, New York, **1994**.
[11] R. J. Shamberger, *Biochemistry of Selenium*, Plenum Press, New York, **1983**.
[12] R. A. Passwaters, *Selenium as Food & Medicine*, Pivot Original Press, New Canaan, **1980**.
[13] Y. Ogasawara, G. Lacourciere, T. C. Stadtman, *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 9494–9498.
[14] Y. Xu, E. T. Kool, *J. Am. Chem. Soc.* **2000**, *122*, 9040–9041.
[15] S. Janzsu, G. Hoppert, J. Shodiere, J.-C. Yerdon, *Jpn. Kokai Tokkyo Koho* JP 11140067, **1999**; *Chem. Abstr.* **1999**, *131*, 32054.
[16] H. E. Ganther, *Bioorg. Med. Chem.* **2001**, *9*, 1459–1466.
[17] G. Mugesh, W.-W. Du Mont, H. Sies, *Chem. Rev.* **2001**, *101*, 2125–2179.
[18] S. W. May, *Exp. Opin. Invest. Drugs* **2002**, *11*, 1261–1269.
[19] E. V. Ratushnaya, Y. I. Kirova, M. A. Suchkov, B. I. Drevko, V. B. Borodulin, *Pharm. Chem. J.* **2002**, *36*, 652–653.
[20] D. L. Hatfield, *Selenium. Its Molecular Biology and Role in Human Health*, Kluwer Academic Publishers, Boston, **2001**.
[21] K. El-Bayoumy, R. Sinha, *Mutat. Res.* **2004**, *551*, 181–197.
[22] C. Ip, M. Birringer, E. Block, M. Kotrebai, J. F. Tyson, P. C. Uden, D. J. Lisk, *J. Agric. Food Chem.* **2000**, *48*, 2062–2070.
[23] J. Lintschinger, N. Fuchs, J. Moser, D. Kuehnelt, W. Goessler, *J. Agric. Food Chem.* **2000**, *48*, 5362–5368.
[24] V. Poggi, A. Arcioni, P. Filippini, P. G. Pifferi, *J. Agric. Food Chem.* **2000**, *48*, 4749–4751.
[25] P. Ximenez-Embun, I. Alonso, Y. Madrid-Albarran, C. Camara, *J. Agric. Food Chem.* **2004**, *52*, 832–838.
[26] D. B. Vickerman, J. T. Trumble, G. N. George, I. J. Pickering, H. Nichol, *Environ. Sci. Technol.* **2004**, *38*, 3581–3586.
[27] R. S. Garigipati, S. M. Weinreb, *1,2-Thiazines and their Benzo Derivatives*, in *Compr. Heterocycl. Chem. II* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Amsterdam, **1996**, vol. 6, pp. 349–382.
[28] M. Sainsbury, *1,3-Oxazines and their Benzo Derivatives*, in *Compr. Heterocycl. Chem. II* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Amsterdam, **1996**, vol. 6, pp. 301–348.
[29] T. L. Gilchrist, J. E. Wood, *1,2-Oxazines and their Benzo Derivatives*, in *Compr. Heterocycl. Chem. II* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Amsterdam, **1996**, vol. 6, pp. 279–299.
[30] Z. J. Witczak, *Tetrahedron* **1985**, *41*, 4781–4785.
[31] W. J. Stec, K. Lesiak, M. Sudol, *Synthesis* **1975**, *12*, 785–787.
[32] K. Sukata, *J. Org. Chem.* **1989**, *54*, 2015–2018.
[33] M. L. Petrov, N. I. Zmitrovich, *Russ. J. Gen. Chem.* **1999**, *69*, 245–256.
[34] a) D. H. R. Barton, S. I. Parekh, M. Tajbakhsh, E. A. Theodorakis, C.-L. Tse, *Tetrahedron* **1994**, *50*, 639–654; b) M. T. Bakhsh, Y. S. Behshtiha, M. M. Heravi, *J. Chem. Soc. Pakistan* **1996**, *18*, 159–162.
[35] M. Koketsu, H. Ishihara, M. Hatsu, *Res. Commun. Mol. Path. Pharm.* **1998**, *101*, 179–186.
[36] M. Koketsu, H. Ishihara, W. Wu, K. Murakami, I. Saiki, *Eur. J. Pharm. Sci.* **1999**, *9*, 157–161.
[37] S. I. Cho, M. Koketsu, H. Ishihara, M. Matsushita, A. C. Nairn, H. Fukazawa, Y. Uehara, *Biochim. Biophys. Acta* **2000**, *1475*, 207–215.
[38] W. Wu, K. Murakami, M. Koketsu, Y. Yamada, I. Saiki, *Anticancer Res.* **1999**, *19*, 5375–5382.
[39] M. Sainsbury, *Selenazines and Benzoselenazines*, in *Rodd's Chemistry of Carbon Compounds*, 2nd ed., Elsevier, Amsterdam, The Netherlands, **1998**, vol. 4 (G/H), pp. 609–621.
[40] M. Sainsbury, *Six-membered rings with two or more heteroatoms with at least one selenium or tellurium*, in *Compr. Heterocycl. Chem. II* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Oxford, **1996**, vol. 6, pp. 987–1018.
[41] a) E. Bulka, H.-G. Patzwaldt, K.-F. Peper, H. Beyer, *Chem. Ber.* **1961**, *94*, 2759–2763; b) E. Bulka, M. Mörner, H. Beyer, *Chem. Ber.* **1961**, *94*, 2763–2768; c) E. Bulka, W. Dietz, H.-G. Patzwaldt, H. Beyer, *Chem. Ber.* **1963**, *96*, 1996–2007.
[42] R. Singh, *Synthetic Dyes*, Mittal Publications, New Delhi, **2002**.
[43] M. J. Parnham, E. Graf, *Prog. Drug. Res.* **1991**, *36*, 9–47.
[44] P. C. Srivastava, R. K. Robins, *J. Med. Chem.* **1983**, *26*, 445–448.
[45] K. Banert, C. Toth, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1627–1629.
[46] H. Maeda, N. Kambe, N. Sonoda, S.-I. Fujiwara, T. Shin-ike, *Tetrahedron* **1997**, *53*, 13667–13680.
[47] a) I. N. Azerbaev, L. A. Tsoi, S. T. Cholpankulova, A. B. Asmanova, V. I. Artyukhin, *Khim. Geterosikl. Soedin.* **1978**, *7*, 917–920; b) I. N. Azerbaev, L. A. Tsoi, A. D. Salimbaeva, S. T. Cholpankulova, G. A. Ryskieva, L. T. Kalkabaeva, M. Z. Aitkhozhaeva, *Tr. Inst. Khim. Nauk., Akad. Nauk. Kaz. SSR* **1980**, *52*, 128–146; *Chem. Abstr.* **1981**, *94*, 208766c.
[48] a) S. Bilinski, T. Urban, *Acta Polon. Pharm.* **1975**, *2*, 159–164; b) S. Bilinski, T. Urban, *Acta Polon. Pharm.* **1976**, *3*, 343–347; c) S. Bilinski, J. Chmielewski, D. Misiuna, T. Urban, *Acta Polon. Pharm.* **1979**, *3*, 307–313.
[49] P. N. Hashim Nizar, S. Parkash, S. M. S. Chauhan, *J. Indian Chem. Soc.* **1997**, *74*, 161–162.
[50] P. K. Atanassov, A. Linden, H. Heimgartner, *Heterocycles* **2003**, *61*, 569–579.
[51] P. K. Atanassov, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2003**, *86*, 3235–3243.
[52] P. K. Atanassov, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2004**, *87*, 1873–1887.

[53] P. K. Atanassov, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2004**, *87*, 1452–1466.
[54] P. K. Atanassov, A. Linden, H. Heimgartner, *Heterocycles* **2004**, *62*, 521–533.
[55] P. K. Atanassov, Y. Zhou, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2002**, *85*, 1102–1117.
[56] Y. Zhou, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 539–553.
[57] Y. Zhou, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 1576–1598.
[58] C. K. Johnson, *ORTEPII*, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee, **1976**.
[59] J. Bernstein, R. E. Davis, L. Shimoni, N.-L. Chang, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1555–1573.
[60] A. R. Katritzky, R. L. Parris, E. S. Ignatchenko, S. M. Allin, M. Siskin, *J. Prakt. Chem.* **1997**, *339*, 59–65.
[61] CCDC-261447–261451 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[62] R. Hooft, *KappaCCD Collect Software*, Nonius BV, Delft, The Netherlands, **1999**.
[63] Z. Otwinowski, W. Minor, in *Methods in Enzymology*, vol. 276 (*Macromolecular Crystallography*), Part A (Eds.: C. W. Carter Jr., R. M. Sweet), Academic Press, New York, **1997**, pp. 307–326.
[64] R. H. Blessing, *Acta Crystallogr. Sect. A* **1995**, *51*, 33–38.
[65] *SIR92*: A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Crystallogr.* **1994**, *27*, 435–436.
[66] A. L. Spek, *PLATON, Program for the Analysis of Molecular Geometry*, University of Utrecht, The Netherlands, **2004**.
[67] a) H. D. Flack, G. Bernardinelli, *Acta Crystallogr. Sect. A* **1999**, *55*, 908–915; b) H. D. Flack, G. Bernardinelli, *J. Appl. Crystallogr.* **2000**, *33*, 1143–1148.
[68] E. N. Maslen, A. G. Fox, M. A. O'Keefe, in *International Tables for Crystallography* (Ed.: A. J. C. Wilson), Kluwer Academic Publishers, Dordrecht, **1992**, vol. C, Table 6.1.1.1, pp. 477–486.
[69] R. F. Stewart, E. R. Davidson, W. T. Simpson, *J. Chem. Phys.* **1965**, *42*, 3175–3187.
[70] J. A. Ibers, W. C. Hamilton, *Acta Crystallogr.* **1964**, *17*, 781–782.
[71] D. C. Creagh, W. J. McAuley, in *International Tables for Crystallography* (Ed.: A. J. C. Wilson), Kluwer Academic Publishers, Dordrecht, **1992**, vol. C, Table 4.2.6.8, pp. 219–222.
[72] D. C. Creagh, J. H. Hubbell, in *International Tables for Crystallography* (Ed.: A. J. C. Wilson), Kluwer Academic Publishers, Dordrecht, **1992**, vol. C, Table 4.2.4.3, pp. 200–206.
[73] G. M. Sheldrick, *SHELXL97, Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, **1997**.

Received: February 3, 2005

